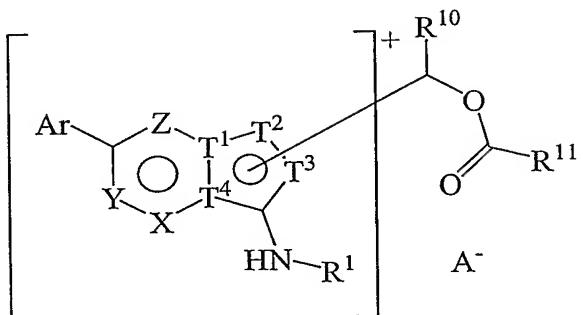


CLAIMS

1. A compound of formula (I):



5

(I)

wherein:

one of T<sup>1</sup> and T<sup>4</sup> is N and the other is C;

one of T<sup>2</sup> and T<sup>3</sup> is N and the other is C(CH<sub>2</sub>)<sub>n</sub>R<sup>2</sup> or N;

10 X, Y and Z are independently N or C(CH<sub>2</sub>)<sub>n</sub>R<sup>3</sup>;

R<sup>1</sup> is Ar<sup>1</sup> or R<sup>1</sup> is C<sub>1-6</sub>alkyl optionally substituted with one or two groups Ar<sup>1</sup>;

Ar<sup>1</sup> is cyclohexyl, piperidinyl, piperazinyl, morpholinyl, adamantyl, phenyl, naphthyl, a six-membered heteroaromatic ring containing one, two or three nitrogen atoms, a five-membered heteroaromatic ring containing one, two, three or four

15 heteroatoms chosen from O, N and S, at most one O or S atom being present, or a nine- or ten-membered bicyclic heteroaromatic ring in which phenyl or a six-membered heteroaromatic ring as defined above is fused to a six- or five-membered heteroaromatic ring as defined above;

Ar<sup>1</sup> is optionally substituted by one, two or three groups chosen from halogen, 20 hydroxy, cyano, nitro, isonitrile, CF<sub>3</sub>, OCF<sub>3</sub>, SF<sub>5</sub>, C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkylthio, C<sub>1-6</sub>alkylsulfinyl, C<sub>1-6</sub>alkylsulfonyl, -NR<sup>6</sup>R<sup>7</sup>, CONR<sup>6</sup>R<sup>7</sup>, -COH, -CO<sub>2</sub>H, C<sub>1-6</sub>alkylcarbonyl, C<sub>1-6</sub>alkoxycarbonyl, haloC<sub>1-6</sub>alkyl, haloC<sub>2-6</sub>alkenyl, haloC<sub>1-6</sub>alkoxy, hydroxyC<sub>1-6</sub>alkyl, aminoC<sub>1-6</sub>alkyl, cyanoC<sub>1-6</sub>alkyl, C<sub>3-6</sub>cycloalkyl, hydroxyC<sub>3-6</sub>cycloalkyl, aminoC<sub>3-6</sub>cycloalkyl, haloC<sub>3-6</sub>cycloalkyl, cyanoC<sub>3-6</sub>cycloalkyl, 25 haloC<sub>1-6</sub>alkylcarbonyl, C<sub>1-6</sub>alkoxycarbonylC<sub>1-6</sub>alkyl, (halo)(hydroxy)C<sub>1-6</sub>alkyl, (halo)(hydroxy)C<sub>3-6</sub>cycloalkyl, phenyl and a five-membered heteroaromatic ring

containing one, two or three heteroatoms, at most one O or S atom being present; wherein the phenyl and five-membered heteroaromatic ring are optionally substituted by C<sub>1-6</sub>alkyl, halo, hydroxy or cyano; when two C<sub>1-6</sub>alkyl groups substitute adjacent positions on Ar<sup>1</sup> then, together with the carbon atoms to which they are attached, they 5 may form a partially saturated ring containing five or six carbon atoms; when two C<sub>1-6</sub>alkoxy groups substitute adjacent positions on Ar<sup>1</sup> then, together with the carbon atoms to which they are attached, they may form a partially saturated five- or six-membered ring;

Ar is phenyl, a six-membered heteroaromatic ring containing one, two or three 10 nitrogen atoms or a five-membered heteroaromatic ring containing one, two, three or four heteroatoms chosen from O, N and S, at most one heteroatom being O or S, Ar being optionally substituted by one, two or three groups chosen from halogen, CF<sub>3</sub>, OCF<sub>3</sub>, C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, nitro, cyano, isonitrile, hydroxy, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkylthio, -NR<sup>6</sup>R<sup>7</sup>, -CONR<sup>6</sup>R<sup>7</sup>, -COH, CO<sub>2</sub>H, C<sub>1-6</sub>alkoxycarbonyl, haloC<sub>1-6</sub>alkyl, 15 haloC<sub>1-6</sub>alkoxy, hydroxyC<sub>1-6</sub>alkyl, aminoC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkylcarbonyl and a five-membered heteroaromatic ring containing one, two, three or four heteroatoms chosen from O, N and S, at most one heteroatom being O or S, optionally substituted by C<sub>1-6</sub>alkyl, halogen, amino, hydroxy or cyano;

R<sup>2</sup> and R<sup>3</sup> are independently hydrogen, halogen, CF<sub>3</sub>, OCF<sub>3</sub>, C<sub>1-6</sub>alkyl, 20 C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, nitro, cyano, isonitrile, hydroxy, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkylthio, -NR<sup>6</sup>R<sup>7</sup>, -CONR<sup>6</sup>R<sup>7</sup>, -COH, CO<sub>2</sub>H, C<sub>1-6</sub>alkoxycarbonyl, haloC<sub>1-6</sub>alkyl, hydroxyC<sub>1-6</sub>alkyl, aminoC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkylaminoC<sub>1-6</sub>alkyl, di(C<sub>1-6</sub>alkyl)aminoC<sub>1-6</sub>alkyl, amido, piperidinyl, piperazinyl, C<sub>3-6</sub>cycloalkyl, morpholinyl, phenyl, a six-membered heteroaromatic ring containing one, two or three 25 nitrogen atoms or a five-membered heteroaromatic ring containing one, two, three or four heteroatoms chosen from O, N and S, at most one O or S atom being present, which phenyl, six-membered heteroaromatic ring and five-membered heteroaromatic ring are optionally substituted by haloC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyl, hydroxy, halogen, amino or cyano;

R<sup>6</sup> and R<sup>7</sup> are independently hydrogen or C<sub>1-6</sub>alkyl; when both R<sup>6</sup> and R<sup>7</sup> are C<sub>1-6</sub>alkyl then, together with the nitrogen atom to which they are attached, they may form a five or six membered saturated nitrogen containing ring;

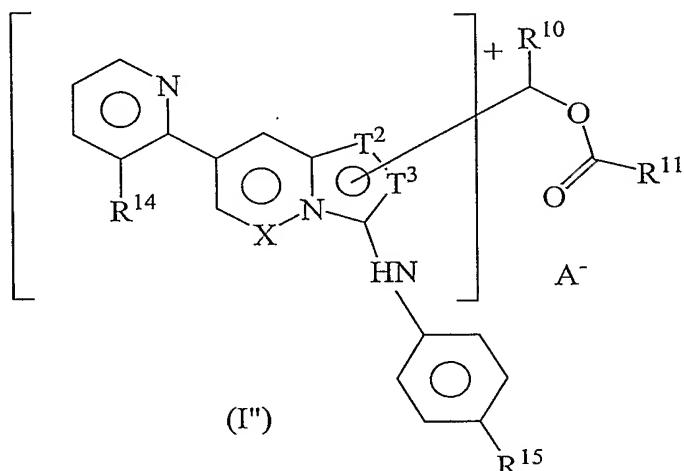
n is zero, one, two or three;

R<sup>10</sup> and R<sup>11</sup> are independently hydrogen, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, C<sub>3-6</sub>cycloalkyl or NR<sup>12</sup>R<sup>13</sup>;

R<sup>12</sup> and R<sup>13</sup> are independently hydrogen or C<sub>1-6</sub>alkyl or R<sup>12</sup> and R<sup>13</sup>, together with the nitrogen atom to which they are attached, may form a nitrogen containing heterocycle; and

5 A<sup>-</sup> is a pharmaceutically acceptable anion.

2. A compound according to claim 1 of formula (I''):



10

wherein:

X is CH or N;

one of T<sup>2</sup> and T<sup>3</sup> is N and the other is C(CH<sub>2</sub>)<sub>n</sub>R<sup>2</sup>;

15 R<sup>2</sup> is hydrogen, halogen, CF<sub>3</sub>, OCF<sub>3</sub>, C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, nitro, cyano, isonitrile, hydroxy, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkylthio, -NR<sup>6</sup>R<sup>7</sup>, -CONR<sup>6</sup>R<sup>7</sup>, -COH, CO<sub>2</sub>H, C<sub>1-6</sub>alkoxycarbonyl, haloC<sub>1-6</sub>alkyl, hydroxyC<sub>1-6</sub>alkyl, aminoC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkylaminoC<sub>1-6</sub>alkyl, di(C<sub>1-6</sub>alkyl)aminoC<sub>1-6</sub>alkyl, amido, piperidinyl, piperazinyl, C<sub>3-6</sub>cycloalkyl, morpholinyl, phenyl, a six-membered heteroaromatic ring containing one, two or three nitrogen atoms or a five-membered heteroaromatic ring containing one, two, three or four heteroatoms chosen from O, N and S, at most one O or S atom being present, which phenyl, six-membered heteroaromatic ring and five-membered heteroaromatic ring are optionally substituted by haloC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyl, hydroxy, halogen, amino or cyano;

- 50 -

$R^6$  and  $R^7$  are independently hydrogen or  $C_{1-6}$ alkyl; when both  $R^6$  and  $R^7$  are  $C_{1-6}$ alkyl then, together with the nitrogen atom to which they are attached, they may form a five or six membered saturated nitrogen containing ring;

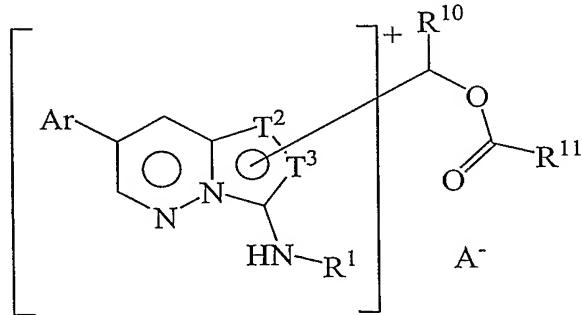
$n$  is zero, one, two or three;

5  $R^{10}$  and  $R^{11}$  are independently hydrogen,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $C_{3-6}$ cycloalkyl or  $NR^{12}R^{13}$  where  $R^{12}$  and  $R^{13}$  are independently hydrogen or  $C_{1-6}$ alkyl or  $R^{12}$  and  $R^{13}$ , together with the nitrogen atom to which they are attached, form a nitrogen-containing heterocycle;

10  $R^{14}$  and  $R^{15}$  are independently  $C_{1-6}$ alkyl,  $CF_3$ , halo $C_{1-6}$ alkyl, halogen,  $C_{1-6}$ alkoxy, halo $C_{1-6}$ alkoxy or  $OCF_3$ ; and

$A^-$  is a pharmaceutically acceptable anion.

3. A compound according to claim 1 of formula (IA):



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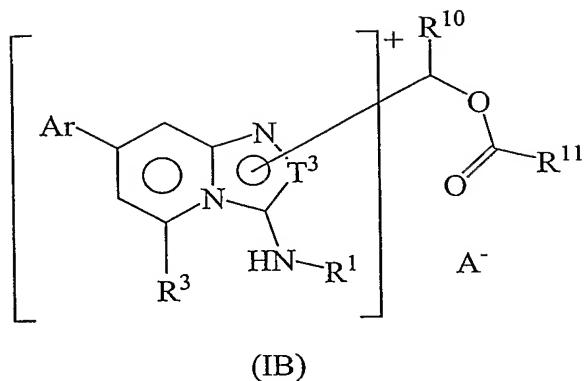
(IA)

wherein  $T^2$ ,  $T^3$ ,  $Ar$ ,  $R^1$ ,  $R^{10}$ ,  $R^{11}$  and  $A^-$  are as defined in claim 1.

4. A compound according to claim 1 of formula (IB):

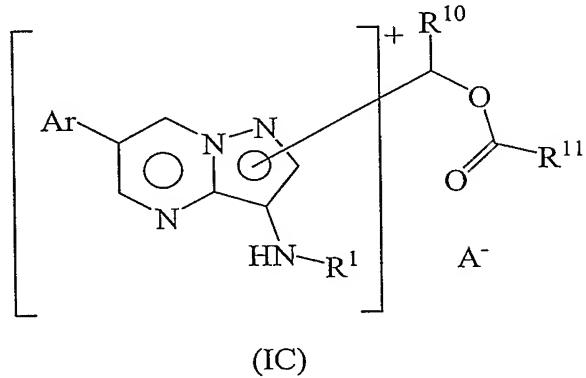
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- 51 -



wherein Ar, R<sup>1</sup>, R<sup>3</sup>, T<sup>3</sup>, R<sup>10</sup>, R<sup>11</sup> and A<sup>-</sup> are as defined in claim 1.

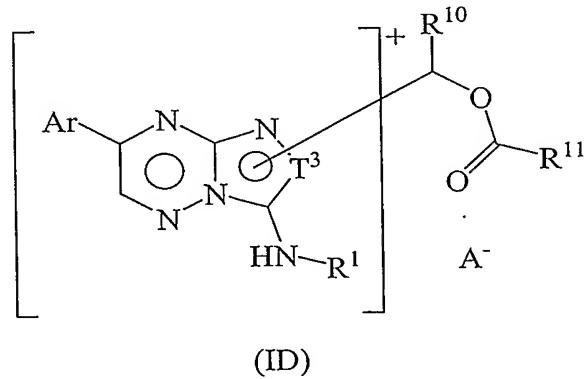
5 5. A compound according to claim 1 of formula (IC):



wherein Ar, R<sup>1</sup>, R<sup>10</sup>, R<sup>11</sup> and A<sup>-</sup> are as defined in claim 1.

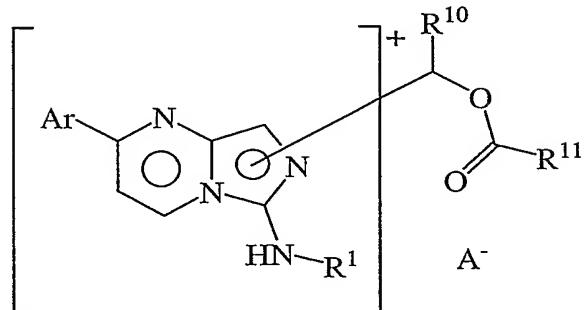
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6. A compound according to claim 1 of formula (ID):



wherein Ar, R<sup>1</sup>, T<sup>3</sup>, R<sup>10</sup>, R<sup>11</sup> and A<sup>-</sup> are as defined in claim 1.

7. A compound according to claim 1 of formula (IE):



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(IE)

wherein Ar, R<sup>1</sup>, R<sup>10</sup>, R<sup>11</sup> and A<sup>-</sup> are as defined in claim 1.

8. A pharmaceutical composition comprising one or more compounds according to any one of claims 1 to 7 in association with a pharmaceutically acceptable carrier or excipient.

9. A compound according to any one of claims 1 to 7 for use in treatment of the human or animal body.

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10. A compound according to any one of claims 1 to 7 for use in the manufacture of a medicament for the treatment or prevention of physiological disorders that may be ameliorated by modulating VR1 activity.

20 11. A compound according to any one of claims 1 to 7 for use in the manufacture of a medicament for the treatment or prevention of a disease or condition in which pain and/or inflammation predominates.

25 12. A method for the treatment or prevention of physiological disorders that may be ameliorated by modulating VR1 activity, which method comprises administration

to a patient in need thereof of an effective amount of a compound of claim 1 or a composition comprising a compound of claim 1.

13. A method for the treatment or prevention of a disease or condition in which  
5 pain and/or inflammation predominates, which method comprises administration to a patient in need thereof of an effective amount of a compound of claim 1 or a composition comprising a compound of claim 1.